

What is claimed is:

1. A method for introducing an intact oligonucleotide into a mammal,

5 the method comprising the step of orally administering to the mammal a chimeric oligonucleotide, the oligonucleotide comprising about 6 to 50 nucleotides linked via at least one phosphorothioate internucleotide linkage and at
10 least one internucleotide linkage selected from the group consisting of alkylphosphonate, phosphorodithioate, alkylphosphonothioate, phosphoramidate, phosphoramidite, phosphate ester, carbamate, carbonate, phosphate triester,
15 acetamidate, and carboxymethyl ester,

whereby the oligonucleotide is present in intact form in plasma at least six hours following oral administration.

20 2. The method of claim 1 wherein the oligonucleotide comprises at least one alkylphosphonate internucleotide linkage.

25 3. The method of claim 2 wherein the oligonucleotide comprises at least one alkylphosphonate internucleotide linkage at its 3' and/or 5' terminal end.

30 4. The method of claim 3 wherein the oligonucleotide comprises at least two alkylphosphonate internucleotide linkages at its 3' and 5' terminal ends.

5. The method of claim 2 wherein the oligonucleotide comprises at least one methylphosphonate internucleotide linkage.

5 6. The method of claim 4 wherein the alkyl phosphonate internucleotide linkage is a methylphosphonate internucleotide linkage.

7. The method of claim 1 wherein the
10 oligonucleotide comprises about from 15 to 25 nucleotides.

8. The method of claim 1 wherein the
15 oligonucleotide is complementary to a gene of a virus, pathogenic organism, or a cellular gene.

12. The method of claim 11 wherein the
oligonucleotide is complementary to a gene of a
virus involved in a disease selected from the
20 group consisting of AIDS, oral and genital herpes,
papilloma warts, influenza, foot and mouth
disease, yellow fever, chicken pox, shingles,
adult T-cell leukemia, Burkitt's lymphoma,
nasopharyngeal carcinoma, and hepatitis.

25 13. The method of claim 1 wherein the
oligonucleotide is complementary to a gene
encoding a protein associated with Alzheimer's
disease.

30

14. The method of claim 1 wherein the oligonucleotide is complementary to a gene encoding a protein in a parasite causing a parasitic disease selected from the group consisting of amebiasis, Chagas' disease, toxoplasmosis, pneumocytosis, giardiasis, cryptosporidiosis, trichomoniasis, malaria, ascariasis, filariasis, trichinosis, schistosomiasis infections.

10